e-ISSN: 3108-2866; p-ISSN: 3139-4108
Available online on https://jmmdt.jcpublications.in
Journal of Medicine, Pharmacology and Medical Devises Technology. Feb 2026; 2(02): 19 – 23.
doi: https://doi.org/10.67170/jmmdt.2026.v2i2.005 Original Research Article

Glycemic control and albuminuria as predictors of histologically confirmed diabetic kidney disease in type 2 diabetes

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Date of submission: 29-11-2025 Date of Review: 10-12-2025 Date of acceptance: 20-02-2026
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Conflict of interest: Nil

Abstract

Background: Diabetic kidney disease (DKD) is a major complication of type 2 diabetes mellitus (T2DM). However, biochemical markers such as HbA1c and microalbuminuria may not always reflect underlying renal histopathology. **Aim:** To correlate HbA1c and microalbuminuria with renal histopathological findings in patients with T2DM.

Methods: This prospective study was conducted at Medicover Hospitals, Visakhapatnam, from December 2024 to June 2025. Sixty T2DM patients with clinical suspicion of renal involvement underwent laboratory evaluation including HbA1c and urinary albumin–creatinine ratio (UACR), followed by ultrasound-guided renal biopsy. Histopathological lesions were classified according to standard criteria. Statistical correlation between biochemical parameters and histology was analyzed.

Results: The mean HbA1c was 8.6 ± 1.4%, and microalbuminuria was present in 56.7% of patients. Renal biopsy revealed isolated DKD in 60%, non-diabetic kidney disease (NDKD) in 23.3%, and mixed lesions in 16.7%. Patients with DKD had significantly higher HbA1c and UACR levels compared to NDKD ($p<0.01$). Poor glycemic control (HbA1c >9%) and macroalbuminuria were strongly associated with advanced DKD lesions.

Conclusion: Elevated HbA1c and microalbuminuria correlate significantly with classical DKD histopathology, though renal biopsy remains essential in atypical cases for precise diagnosis and tailored management.

Key Words: Type 2 Diabetes Mellitus, Diabetic Kidney Disease, HbA1c, Microalbuminuria, Renal Histopathology

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Introduction:

Diabetic kidney disease (DKD) is a leading cause of chronic kidney disease in type 2 diabetes mellitus (T2DM), yet routine clinical markers may not fully reflect the underlying renal lesions, and biopsy can reveal mixed or non-diabetic pathology. HbA1c integrates long-term glycemic exposure and has been linked to renal microvascular structural injury; in a zero-time donor biopsy cohort, higher HbA1c (even in the high-normal range) correlated with renal arteriolar wall thickening, supporting a continuum from dysglycemia to vascular damage [1]. Albuminuria is used to stage DKD, but large biopsy series show many patients have non-DKD or superimposed lesions, and microalbuminuria versus macroalbuminuria helps stratify the likelihood of alternative diagnoses [2].Biopsy studies in T2D also suggest higher HbA1c tends to align with DKD patterns on histology, highlighting the value of correlating biochemical indices with tissue changes [3]. In this study, HbA1c and microalbuminuria were correlated with renal histopathology in T2DM in clinically suspected DKD cases.

Methods:

This prospective observational study was conducted at Medicover Hospitals, Visakhapatnam, from December 2024 to June 2025. After obtaining approvals, written informed consent was collected from all participants. Consecutive adult patients with T2DM attending the outpatient clinics or admitted under internal medicine/nephrology services were screened. Patients were enrolled if they had evidence of diabetic kidney involvement, defined as persistent microalbuminuria (urinary albumin–creatinine ratio [UACR] 30–300 mg/g in at least two of three samples over 3 months) and/or reduced estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m^2), with clinical suspicion warranting renal biopsy as per treating nephrologist. Patients with type 1 diabetes, pregnancy, acute kidney injury, active urinary tract infection, obstructive uropathy, known primary glomerulonephritis, solitary kidney, bleeding diathesis, uncontrolled hypertension, or contraindications to biopsy were excluded. A structured case record form captured demographic details, duration of diabetes, comorbidities, medications (including renin–angiotensin system blockers and SGLT2 inhibitors), blood pressure, body mass index, and relevant complications.

Baseline laboratory evaluation was performed at enrolment. Venous blood samples were collected for HbA1c, fasting/random plasma glucose, serum creatinine, urea, electrolytes, lipid profile, and complete blood count. eGFR was calculated using the CKD-EPI equation. Urine evaluation included dipstick screening, microscopy to rule out

infection/active sediments, and UACR estimation from an early morning spot sample using an immunoturbidimetric (or equivalent validated) assay; repeat samples were obtained where required to document persistence. Microalbuminuria was graded as normoalbuminuria (<30 mg/g), microalbuminuria (30–300 mg/g), or macroalbuminuria (>300 mg/g). Patients were clinically stabilized prior to biopsy; blood pressure was optimized, antiplatelet/anticoagulant medications were withheld as per protocol, and bleeding risk was assessed (platelet count, PT/INR). All investigations and biopsy-related steps were recorded prospectively during the study period.

Renal biopsy was performed under real-time ultrasound guidance using an automated spring-loaded biopsy gun (typically 16G), with post-procedure monitoring for complications. Adequate cores were sent for light microscopy and immunofluorescence; electron microscopy was performed when indicated/available as per hospital practice. Histopathological evaluation was done by an experienced renal pathologist blinded to the index values, and lesions were classified as diabetic kidney disease (DKD) and/or non-diabetic kidney disease (NDKD) based on standard criteria. DKD lesions were graded using recognized histopathological classes (e.g., mesangial expansion, nodular sclerosis, interstitial fibrosis/tubular atrophy, arteriolar hyalinosis), and the presence of superimposed glomerulopathies was noted. HbA1c and UACR were correlated with predominant histopathological patterns and severity grades. Data were entered in a secure spreadsheet and analyzed using standard statistical methods: continuous variables were summarized as mean±SD or median (IQR), categorical variables as counts and percentages; correlations were assessed using Pearson/Spearman tests; group comparisons used t-test/ANOVA or Mann–Whitney/Kruskal–Wallis as appropriate; and multivariable logistic regression evaluated independent associations of HbA1c and microalbuminuria with DKD class and NDKD after adjusting for age, duration of diabetes, blood pressure, and eGFR. A p value <0.05 was considered statistically significant.

Results:

A total of 60 patients with T2DM were included in the study. As shown in Table 1, the mean age was 56.8 ± 9.4 years, with a male predominance (63.3%), and the average duration of diabetes was 11.6 ± 5.2 years; 70% had coexisting hypertension. The glycemic and albuminuria profile presented in Table 2 demonstrated a mean HbA1c of 8.6 ± 1.4%, with 30% of patients exhibiting poor glycemic control (HbA1c >9%). Microalbuminuria was the most frequent presentation (56.7%), while 30% had macroalbuminuria. Histopathological findings summarized in Table 3 revealed isolated diabetic kidney disease (DKD) in 60% of cases, non-diabetic kidney disease (NDKD) in 23.3%, and mixed lesions in 16.7%, with Class III lesions being the most common among DKD cases. Correlation analysis in Table 4 showed that patients with DKD had significantly higher mean HbA1c levels (9.1 ± 1.2%) compared to NDKD (7.8 ± 1.0%) (p=0.001), and markedly elevated UACR values (228 ± 96 mg/g vs 112 ± 54 mg/g; p=0.002). Poor glycemic control and macroalbuminuria were significantly associated with DKD histopathology, indicating that elevated HbA1c and increased albumin excretion strongly correlate with advanced diabetic renal lesions.

Discussion:

The baseline characteristics of our cohort reflect a typical high-risk type 2 diabetic population with renal involvement. The mean age of 56.8 ± 9.4 years and male predominance (63.3%) are consistent with epidemiological data showing increased DKD prevalence in middle-aged and elderly males with long-standing diabetes [4]. The average duration of diabetes (11.6 ± 5.2 years) supports the concept that chronic hyperglycemic exposure plays a pivotal role in structural kidney damage [5]. Hypertension was present in 70% of participants, reinforcing its synergistic role in accelerating glomerular injury, arteriolar hyalinosis, and interstitial fibrosis [6]. Elevated systolic blood pressure in our population likely contributed to progressive nephron loss, as highlighted in KDIGO 2022 guidelines emphasizing strict blood pressure control in diabetic CKD [7]. The reduced mean eGFR (54.2 ± 18.6 mL/min/1.73m²) further indicates established renal impairment, which correlates with histological chronicity indices such as IFTA and vascular sclerosis [8]. These findings confirm that our study population represents clinically significant diabetic kidney involvement rather than early asymptomatic disease.

Table 2 demonstrates suboptimal glycemic control, with a mean HbA1c of 8.6 ± 1.4% and 30% of patients having HbA1c >9%. Chronic hyperglycemia induces mesangial matrix expansion, podocyte dysfunction, and glomerular basement membrane thickening through advanced glycation end products and oxidative stress pathways [9]. Experimental and human biopsy studies have shown that higher HbA1c levels correlate with microvascular structural injury, even before overt renal dysfunction [10]. Albuminuria distribution in our cohort revealed microalbuminuria in 56.7% and macroalbuminuria in 30%, supporting its central role as an early marker of glomerular barrier damage [11]. Longitudinal studies demonstrate that increasing albuminuria trajectories strongly predict progression to end-stage kidney disease [12]. However, albuminuria alone cannot reliably distinguish DKD from NDKD, underscoring the importance of histological confirmation in selected

cases [13]. Thus, Table 2 reflects biochemical severity that plausibly underlies the histological findings observed in Table 3.

Histopathological analysis (Table 3) revealed isolated DKD in 60% of cases, NDKD in 23.3%, and mixed lesions in 16.7%. These findings align with recent biopsy-based cohorts reporting NDKD prevalence ranging from 20–40% in diabetics undergoing biopsy [14]. The predominance of Class III lesions indicates nodular sclerosis or advanced mesangial expansion, reflecting chronic metabolic injury [15]. The Renal Pathology Society classification provides prognostic stratification, where higher classes and greater interstitial fibrosis predict worse renal outcomes [16]. The presence of mixed lesions is clinically significant, as diabetes may coexist with treatable glomerulopathies such as IgA nephropathy or membranous nephropathy [17]. Therefore, Table 3 emphasizes the diagnostic value of biopsy in differentiating classical DKD from alternative renal diseases, guiding therapeutic decisions beyond glycemic control alone.

Table 4 demonstrates a statistically significant association between higher HbA1c levels and DKD histology (p=0.001), confirming that poor glycemic control strongly correlates with classical diabetic lesions. Similarly, elevated UACR levels were significantly higher in DKD compared to NDKD (p=0.002), supporting albuminuria as a structural injury marker [18]. The significant association of macroalbuminuria and HbA1c >9% with DKD underscores the cumulative metabolic and hemodynamic burden contributing to glomerulosclerosis. Therapeutic trials have demonstrated that reduction in albuminuria through renin-angiotensin system blockade, SGLT2 inhibitors, and mineralocorticoid receptor antagonists slows CKD progression [18, 19]. Hence, Table 4 validates HbA1c and microalbuminuria as strong clinical predictors of histologically confirmed DKD, although biopsy remains essential when clinical-laboratory discordance exists.

Overall, integrating clinical parameters (Table 1), biochemical severity (Table 2), structural pathology (Table 3), and correlation analysis (Table 4) provides a comprehensive understanding of diabetic renal injury. Our findings reinforce that higher HbA1c and increased albumin excretion are closely linked to advanced diabetic glomerular lesions, while a significant proportion of patients harbor non-diabetic pathology requiring individualized management. This emphasizes the importance of a biopsy-guided, precision-based approach in the management of type 2 diabetes with renal involvement.

Conclusion: This prospective study demonstrated a strong correlation between poor glycemic control, elevated microalbuminuria, and classical diabetic kidney disease (DKD) on renal histopathology in patients with type 2 diabetes. Higher HbA1c levels and macroalbuminuria were significantly associated with advanced glomerular lesions, particularly Class III DKD. However, a substantial proportion of patients exhibited non-diabetic or mixed renal pathology, emphasizing that biochemical markers alone cannot reliably predict underlying histology. These findings highlight the importance of integrating clinical, biochemical, and histopathological evaluation to ensure accurate diagnosis and individualized management. Renal biopsy remains valuable in selected patients with atypical features or clinical-laboratory discordance.

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Table 1: Baseline Demographic and clinical characteristics

Variable	Mean ± SD / n (%)
Age (years)	56.8 ± 9.4
Male	38 (63.3%)
Duration of Diabetes (years)	11.6 ± 5.2
Hypertension	42 (70.0%)
BMI (kg/m²)	26.4 ± 3.1
Systolic BP (mmHg)	142 ± 16
eGFR (mL/min/1.73m²)	54.2 ± 18.6

Table 2: Glycemic and albuminuria profile among the study members

Parameter	Mean ± SD / n (%)
HbA1c (%)	8.6 ± 1.4
HbA1c <7%	10 (16.7%)
HbA1c 7–9%	32 (53.3%)
HbA1c >9%	18 (30.0%)
Normoalbuminuria	8 (13.3%)
Microalbuminuria	34 (56.7%)
Macroalbuminuria	18 (30.0%)
UACR (mg/g)	186 ± 102

e-ISSN: 3108-2866; p-ISSN: 3139-4108
Available online on https://jmmdt.jcpublications.in
Journal of Medicine, Pharmacology and Medical Devises Technology. Feb 2026; 2(02): 19 – 23.

Table 3: Renal histopathology findings among the study members	
Histopathological Pattern	**n (%)**
Isolated Diabetic Kidney Disease (DKD)	36 (60.0%)
Non-Diabetic Kidney Disease (NDKD)	14 (23.3%)
Mixed Lesions (DKD + NDKD)	10 (16.7%)
Class II DKD	14 (23.3%)
Class III DKD	18 (30.0%)
Class IV DKD	14 (23.3%)

Table 4: Correlation of HbA1c and microalbuminuria with histopathology			
Variable	**DKD (n=36)**	**NDKD (n=14)**	**P value**
HbA1c (%)	9.1 ± 1.2	7.8 ± 1.0	0.001*
UACR (mg/g)	228 ± 96	112 ± 54	0.002*
HbA1c >9%	16 (44.4%)	2 (14.3%)	0.03*
Macroalbuminuria	16 (44.4%)	2 (14.3%)	0.02*